MicroRNAs in human cardiac aging: therapeutic targets and biomarkers

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Introduction

Cardiovascular diseases

- Aging stress
- Oxidative stress
- Cardiomyocyte
- Fibrosis
- Myocardial hypertrophy
- Ischemic area
- African progenitor and myocyte

MicroRNA (miRNA)

- Regulators of biological processes. Therapeutic targets.
- Actively and passively released to body fluids. Biomarkers.

Role of miRNAs in age-related cardiac remodelling is poorly understood in humans.

Bioinformatic identification of age-related miRNAs (BioAGEmiRNAs) in human left ventricle and their predicted downstream target genes.

Materials and methods

- Luciferase reporter assays conducted in order to validate interactions between BioAGEmiRNAs and cardiac-related genes.
- Description of a new individual transcriptomic age index (Apparent Age, AppAge) in white blood cells (WBC) from young to centenarian human donors adapting published methods2.
- Quantification of expression levels of cardiac-enriched BIOAGE-miRNAs and myo-miRNAs in plasma from healthy young (20-30 y.o.), adult (40-50 y.o.), elder (60-70 y.o.) and centenarian (100 y.o.) donors.

Goals

- Validate the bioinformatic BIOAGEmiRNA regulatory network.
- Investigate miRNAs as indicators of the biological age of the heart.

Results

8 of 23 predicted interactions between miR-24-2-5p, miR-24-2-3p, miR-4435 and miR-3916 and predicted targets are positive

Definition of a transcriptomic biological age index (AppAge) in WBC of the individual

The levels of the studied cardiac-enriched BIOAGE-miRNAs and myo-miRNAs reveal significant (P ≤ 0.05) or nearly significant (P ≤ 0.15) correlation with chronological age and AppAge

Conclusions

- 35% of tested interactions have been validated in vitro. Thus, miRNAs emerge as important regulators of gene expression in age-related cardiac dysfunction.
- AppAge is proposed as a potential indicator of the biological age of an individual.
- Circulating cardiac BIOAGEmiRNAs or myomiRNAs could report biological age of the heart in relation to the chronological and/or AppAge.
- Our data promotes the deciphering of molecular mechanism underlying the process of cardiac aging and its minimal-invasive monitoring in human.

References


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